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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
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Gina N. Shishima
Fulbright & Jaworski L.L.P.
Suite 2400
600 Congress Avenue
Austin, TX 78701

EXAMINER
WILDER, CYNTHIA B

ART UNIT	PAPER NUMBER
1637	

DATE MAILED: 04/15/2003

12

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No. 09/835,082	Applicant(s) Ratain et al.
	Examiner Cynthia B Wilder	Art Unit 1637

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136 (a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133).
- Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1) ☒ Responsive to communication(s) filed on *Feb 5, 2003* .

2a) ☒ This action is **FINAL**. 2b) ☐ This action is non-final.

3) ☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11; 453 O.G. 213.

Disposition of Claims

4) ☒ Claim(s) *1-99* is/are pending in the application.

4a) Of the above, claim(s) *1-76, 85-87, and 95-99* is/are withdrawn from consideration.

5) ☐ Claim(s) _____ is/are allowed.

6) ☒ Claim(s) *77-84 and 88-94* is/are rejected.

7) ☐ Claim(s) _____ is/are objected to.

8) ☐ Claims _____ are subject to restriction and/or election requirement.

Application Papers

9) ☐ The specification is objected to by the Examiner.

10) ☐ The drawing(s) filed on _____ is/are a) ☐ accepted or b) ☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

11) ☐ The proposed drawing correction filed on _____ is: a) ☐ approved b) ☐ disapproved by the Examiner.

If approved, corrected drawings are required in reply to this Office action.

12) ☐ The oath or declaration is objected to by the Examiner.

Priority under 35 U.S.C. §§ 119 and 120

13) ☐ Acknowledgement is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a) ☐ All b) ☐ Some* c) ☐ None of:

1. ☐ Certified copies of the priority documents have been received.
2. ☐ Certified copies of the priority documents have been received in Application No. _____ .
3. ☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

*See the attached detailed Office action for a list of the certified copies not received.

14) ☐ Acknowledgement is made of a claim for domestic priority under 35 U.S.C. § 119(e).

a) ☐ The translation of the foreign language provisional application has been received.

15) ☐ Acknowledgement is made of a claim for domestic priority under 35 U.S.C. §§ 120 and/or 121.

Attachment(s)

1) ☐ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO-1449) Paper No(s). _____
4) ☐ Interview Summary (PTO-413) Paper No(s). _____
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other:

FINAL ACTION

1. Applicant's amendment filed in Paper No. 11 is acknowledged. Claims 77, 79, 80-84, 88, and 90-94 have been amended. Claims 77-84 and 88-94 are pending in the instant application. Claims 85-87 and 95-99 have been withdrawn from consideration as being drawn to a non-elected invention. All of the amendments have been thoroughly reviewed and considered but they are not found persuasive for the reasons that follows. Any rejection not reiterated in this action have been withdrawn as being obviated by the amendment of the claims.

This Action is FINAL.

2. The text of those sections of Title 35, U.S. Code not included in this action can be found in a prior Office action.

Previous Objections and Rejections

3. The objections to the specification is maintained and discussed below. The objection to the claims is withdrawn in view of Applicant's amendment. The claim rejections under 35 U.S.C. 112 first paragraph directed to claims 77-84 and 88-94 as lacking enablement is maintained and discussed below. The claim rejection under 35 U.S.C. 112 first paragraph directed to claims 77-84 and 88-94 as lacking adequate written description is maintained and discussed below. The claim rejection under 35 U.S.C. 112 second paragraph directed to claims 77-84 and 88-94 as being incomplete is maintained and discussed below. The claim rejection under 25 U.S.C. 112 second paragraph directed to claims 77-84 and 88-94 for abbreviations in the claim is withdrawn in view of Applicant's amendment.

Objections

4. Once again, the specification is objected to because the specification contains sequences (primers) at page 113 that are not listed in the sequence listing or CRF and are not represented by a sequence identifier (SEQ ID NO:). Appropriate correction is required.

Claim Rejections - 35 U.S.C. § 112 first paragraph: Lack of Enablement

5. Claims 77-84 and 88-94 are rejected under 35 U.S.C. 112, first paragraph, as containing subject matter which was not described in the specification in such a way as to enable one skilled in the art to which it pertains, or with which it is most nearly connected, to make and/or use the invention. The first paragraph of section 112 requires the specification describe how to make and use the invention. There are many factors to be considered when determining whether there is sufficient evidence to support determination that a disclosure does not satisfy the enablement requirements and whether the necessary experimentation is undue (See *In re Wands*, 858 F. 2d 731, 8 USPQ2d 1400, 1404 (Fed. Cir. 1988)). These factors include, but are not limited to:

I. Quality of Experimentation Necessary

The claimed invention is drawn to a method for evaluating the risk of flavopiridol-induced toxicity in a patient comprising evaluating a UGT1A9-encoding nucleic acid or a ABC-encoding nucleic acid of the patient for a polymorphism. The specification beginning at page 97 discloses well known nucleic acid detection methods for identifying single nucleotide polymorphisms (SNPs). At page 113, the specification discloses a method for identifying a region containing a SCA2-SNP

using PCR amplification procedures. The specification however fails to identify what the SCA2-SNP is or how the SCA2-relates to the method of evaluating the risk of flavopiridol-induced toxicity. In fact, the specification fails to identify or disclose any SNP or polymorphism associated with flavopiridol-induced toxicity. There is no disclosure describing the association of one single SNP or polymorphism to UGT1A9 or to an ABC-encoding nucleic acid. There is no disclosure anywhere in the specification wherein a specific polymorphism is linked to the risk of flavopiridol-induced toxicity. There is no information provided to enable one of ordinary skill in the art to make or use the claimed method as described to evaluate the risk of flavopiridol-induced toxicity since no polymorphisms of the AGT1A9- or ABC-encoding nucleic acid have been identified as it relates to flavopiridol. There is no information to allow one of ordinary skill in the art to make or use the claimed method using the large number of undisclosed polymorphic sequences. As to the quality of experimentation required, one of skill in the art would have to design an experimental procedure to evaluate the risk of flavopiridol-induced toxicity in a patient and to identify polymorphisms of a UGT1A9 or ABC nucleic acid as they relate to flavopiridol.

II. Amount of Direction and Guidance and Presence or Absence of Working Examples

The specification does not provide a method of evaluating the risk of flavopiridol-induced toxicity that bears a reasonable correlation to the entire scope of the claims. The example starting at page 118 does not describe or disclose a single polymorphism that is associated with any nucleic acid or is associated with flavopiridol. The examples merely teach patient treatment with a flavopiridol compound, pharmacokinetics for quantitating flavopiridol in plasma using HPLC or

metabolism of flavopiridol and statistical analysis. Example 3 suggest pharmacogenetic screening and polymorphism analysis but does not describe or disclose how the polymorphic analysis occurs or detection of any polymorphism. There is no indication from the specification wherein a polymorphism is responsible for flavopiridol-induced toxicity in any patient or animal. No example is given wherein a polymorphism of the UGT1A9 -encoding nucleic acid is detected or wherein a polymorphism of the ABC-encoding nucleic acid is detected wherein the polymorphism is associated with the risk of flavopiridol-induced toxicity. Merely, making reference to polymorphisms of the UGT1A9-encoding nucleic acid and/or the ABC-encoding nucleic acid being associated with flavopiridol induced toxicity does not enable one skill in the art to use the instant invention as claimed. Clearly, the claimed invention provides insufficient guidance and direction and lacks proper working examples for one skilled in the art to make and use the claimed invention without undue experimentation.

III. Nature of the Invention

The nature of the invention is a method for evaluating the risk of flavopiridol-induced toxicity in a patient comprising evaluating a UGT1A9-encoding nucleic acid or ABC-encoding nucleic acid of a patient for a polymorphism. The specification however does not define any polymorphisms of the UGT1A9-encoding nucleic acid or the ABC-encoding nucleic acid. While the specification discloses a SCA2-SNP at page 113, the specification does not disclose or describe what the SNP is or how the SNP relates to the instant invention. To reiterate, merely making reference to methods for detecting SNPs does not enable a person to evaluate the risk of flavopiridol-

induced toxicity by evaluating a UGT1A9-encoding nucleic acid or ABC-encoding nucleic acid for a polymorphism. Furthermore, identifying a polymorphism in a UGT1A9-encoding or ABC-encoding nucleic acid does not necessarily equate to detecting or evaluating toxicity associated with flavopiridol because some polymorphisms may simply be non-functional or silent mutations. Thus further experimentation is required.

IV. Relative skill in art and predictability of the art

The level of skill in molecular biology at the time the invention was made is high, however the level of unpredictability in molecular biology is also high. Although certain relevant techniques useful to the claimed invention were know in the prior art, the prior art does not teach a method for detecting or evaluating the risk of flavopiridol-induced toxicity in a patient by evaluating a UGT1A9-encoding nucleic acid for a polymorphism or by evaluating a ABC-encoding nucleic acid for a polymorphism.

For all of the forgoing reasons, undue experimentation is necessary for one of skill in the art to obtain the claimed invention.

6. Applicant's amendment filed in Paper No. 11 has been thoroughly reviewed and considered but are not found persuasive for the reasons that follows. Applicant traverses the rejection on the following grounds: Applicant states that the enablement requirement is met by describing any mode of enablement of the invention. Applicant states that throughout the specification Applicant have described the UGT1A9 nucleic acids for example, see pages 75-81 of the of the specification.

Applicant states that Applicant have also provided in the sequence listing the nucleic acid sequence of the claimed invention. Applicant states that at pages 24-27, Applicant provided detailed description of flavopiridol, correlation of glucuronidation and flavopiridol toxicity, the role of ATP-binding cassette (ABC) proteins in regulating flavopiridol toxicity, genetic polymorphisms of flavopiridol and the involvement of UDG-glucuronosyltransferase variants in polymorphism of flavopiridol. On page 73-74, Applicants have provided various ABC proteins along with their respective GenBank Accession numbers. At pages 105-117 Applicants have provided more than adequate written description of assay and screening methods for detecting polymorphism. In the Example at page 118-129, Applicant have provides more than adequate description regarding assay of flavopiridol and FLAVO glucuronidation, screening polymorphisms of UGT for FLAVOs glucuronidation, screening polymorphisms of UGT for FLAVO activity, and pharmacogenetic screening and polymorphism analysis to detect FLAVO drug toxicity. Applicant states that figure 7 shows the contribution of UGT isoforms to the formation of FLAVO-G. Applicant states that the Examiner has not shown that the specification is not enabled. Applicant further states the enablement requirement is met by describing any mode of enablement of the invention. Applicant states that the evidence provided makes the rejection moot as lacking enablement from the specification, figures and the sequence listing as described above. Applicant respectfully request the rejection be withdrawn.

7. The arguments of Paper No. 11 have been thoroughly reviewed and considered but are not found persuasive for the reasons that follows: Regarding Applicant's arguments, the claimed

invention is drawn to a method for evaluating the risk of flavopiridol-induced toxicity in a patient comprising evaluating a uridine diphosphate glucuronosyltransferase 1A9 (UGT1A9) encoding nucleic acid of the patient for a polymorphism. However, while it is acknowledged that the specification teaches the nucleic acid sequence of the UGT1A9 and has described the claimed nucleic acid sequence, the specification has not described or disclosed any polymorphisms of the AGT1A9 or ABC encoding nucleic acid. Additionally, while the Examiner acknowledged Applicant's claimed evidence, it is noted that the cited evidence does not support the claimed invention as written. To reiterate the claimed invention is drawn to a method for evaluating the risk of flavopiridol-induced toxicity in a patient comprising evaluating a uridine diphosphate glucuronosyltransferase 1A9 (UGT1A9) encoding nucleic acid of the patient for a polymorphism. However, the specification does not provide a disclosure anywhere wherein a specific polymorphism of the UGT1A9-encoding nucleic acid or in fact, any polymorphism, is linked to, or correlated with a risk flavopiridol-induced toxicity. Furthermore, merely looking for polymorphisms in a UGT1A9-encoding nucleic acid of a patient does not necessary suggest that the polymorphism will be associated with a risk flavopiridol-induced toxicity because some of the polymorphisms detected may be silent, non-functional or may be linked to some other condition not associated with flavopiridol-induced toxicity. Thus without any guidance how is one to determine which of the polymorphisms detected are indeed correlated with a risk of flavopiridol-induced toxicity? Also, how is one to evaluate a nucleic acid sequence, such as UGT1A9-encoding nucleic acid sequence, for polymorphisms to determine a risk of flavopiridol-induced toxicity? Furthermore, the evidence

cited by Applicant does not provide any information to determined which SNPs or polymorphisms of the AGT1A9 or ABC- encoding nucleic acids are considered functional. While it is noted at page 27, that polymorphisms of the ABC transporter have been recently identified in the prior art, this does not support the specification's claim for evaluating the risk of Flavopiridol-induced toxicity in a patient comprising evaluating a UGT1A9-encoding nucleic acid because the specification does not teach the identification of those SNP and their involvement with flavopiridol-induced toxicity or involvement with the UGT1A9-encoding nucleic acid. Thus merely providing a method of screening for SNPs of a gene or nucleic acid sequence does not enable a persons to make or use the claimed invention as written. Still further as noted in the prior Office action, there is no indication from the specification wherein a polymorphism is detected or responsible for flavopiridol-induced toxicity in a patient or animal. There are no examples given wherein at least one polymorphism or SNP of the UGT1A9-encoding nucleic acid is detected and linked to the risk of flavopiridol-induced toxicity. Additionally there is no disclosure suggesting that any SNP of the UGT1A9 sequence will result in a risk of flavopiridol-induced toxicity. To reiterate, identifying any polymorphism in a UGT1A9-encoding or ABC-encoding nucleic acid does not necessarily equate to evaluating toxicity associated with flavopiridol because some polymorphisms may simply be non-functional or silent mutations. Thus contrary to Applicant's argument, undue experimentation is required to one of skill in the art to make or use the claimed invention. Applicant's evidence is not sufficient to overcome the claim rejection under 25 U.S.C. 112 first paragraph as lacking enablement. Accordingly, the rejection is maintained.

Claim Rejections - 35 U.S.C. § 112 first paragraph: Lack of Adequate Written Description

8. Claims 77-84 and 88-94 are rejected under 35 U.S.C. 112, first paragraph, as containing subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention. The claimed invention is drawn to a method for evaluating the risk of flavopiridol-induced toxicity in a patient comprising evaluating a UGT1A9-encoding nucleic acid of the patient for a polymorphism. The claimed invention is also drawn to method for evaluating the risk of flavopiridol-induced toxicity in a patient comprising evaluating a ABC-encoding nucleic acid of the patient for a polymorphism. The disclosure of evaluating a UGT1A9-encoding nucleic acid or ABC-encoding nucleic acid for a polymorphism encompasses a large number of nucleic acid species not describe or disclosed anywhere in the specification. A representative number of species for each genus must be disclosed to meet the written description requirement of 112, first paragraph. As set forth by the Court in *Vas Cath Inc. V. Mahurkar*, 19 USPQ2d 1111, the written description must convey to one of skill in the art "with reasonable clarity" that as of the filing date Applicant was in possession of the claimed invention. Absent a written description disclosing a representative number of the species as claimed in claims 77-84 and 88-94 of the specification fails to show that Applicant was, in fact, "in possession of the claimed invention" at the time the application for patent was filed.

9. Applicant traverses the rejection for similar reasons recited above at #7. Applicant states that adequate written description has been provided to allow one of skill in the art to practice the

claimed invention. Applicant states that throughout the specification Applicant have described the UGT1A9 nucleic acids. Applicant stats that a sequence listing have been provided of the claimed invention and Applicant has provided detail description of flavopiridol, correlation of glucuronidation and flavopiridol toxicity, the role of ATP-binding cassette proteins in regulating flavopiridol toxicity, genetic polymorphisms of flavopiridol, and the involvement of UDG-glucuronosyltransferase variants in polymorphism of flavopiridol. On page 73-74, Applicants have provided various ABC proteins along with their respective GenBank Accession numbers. At pages 105-117 Applicants have provided more than adequate written description of assay and screening methods for detecting polymorphism. In the Example at page 118-129, Applicant have provides more than adequate description regarding assay of flavopiridol and FLAVO glucuronidation, screening polymorphisms of UGT for FLAVOs glucuronidation, screening polymorphisms of UGT for FLAVO activity, and pharmacogenetic screening and polymorphism analysis to detect FLAVO drug toxicity. Applicant states that figure 7 shows the contribution of UGT isoforms to the formation of FLAVO-G. Applicant contends that they have provided an adequate description in the disclosure and working examples to show that they had possession of the invention at the time of filing for application.

9. The arguments of Paper No. 11 have been thoroughly reviewed and considered by they are not found persuasive for the reasons previously discussed above at # 8. To reiterate, the invention is drawn to a method for evaluating the risk of flavopiridol-induced toxicity in a patient comprising evaluating a UGT1A9-encoding nucleic acid or an ABC-encoding nucleic acid of a patient for a

polymorphism. The specification has not disclosed or described or even suggest any polymorphisms of the UGT1A9-encoding nucleic acid or an ABC-encoding nucleic acid that equates to a risk of flavopiridol toxicity. The disclosure of "evaluating a UGT1A9-encoding nucleic acid or an ABC-encoding nucleic acid of a patient for a polymorphism" encompasses a large genus of nucleic acid species not described or disclosed anywhere in the specification. As noted in the prior Office action, a representative number of species for each genus **must** be disclosed to to meet the written description requirement of 112, first paragraph. Applicant has not provided a representative number of species for the genus of the claimed invention because Applicant has not disclosed or described any polymorphism of the said nucleic acid sequences recited in the claims. Applicant has not provided sufficient evidence to overcome the rejection under 35 U.S.C. 112 first paragraph as lacking adequate written description. Accordingly, the rejection is maintained.

Claim Rejections - 35 U.S.C. § 112

10. Claim 77-84 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which Applicant regards as the invention.

(a) Claims 77-84 and 88-94 are incomplete and indefinite in claim 77 because it cannot be determined how evaluating a UGT1A9-encoding nucleic acid or ABC-encoding nucleic acid for a polymorphism relates to evaluating the risk of flavopiridol-induced toxicity. Additionally the term "evaluating" is a non-specific activity and therefore it is unclear how the claimed method operates

to detect the polymorphism". Method claims need not recite all operating details but should at least recite positive, active steps so that the claims will set out and circumscribe a particular area with a reasonable degree of precision and particularity and make clear what subject matter that claims encompass as well as make clear the subject matter from which other would be precluded. *Ex parte Erlich*, 3 USPQ2d 1011 at 6. It is suggested amending the claims at step (a) to recite positive and active method steps.

11. Applicant traverses the rejection on the following grounds: Applicant states that as provided throughout the specification of the application and in the Examples, the variability in flavopiridol to glucuronidation reflects a variability in the genetic differences in isozymes which through pharmacogenetic screening identifies individuals predisposed to flavopiridol toxicity. Applicant states that the specification teaches that glucuronidation of flavopiridol is the major mechanism of flavopiridol transformation. Applicant states that glucuronidation by UGT enzyme is a major drug metabolic pathway in humans. Applicant states that examples of UGT enzymes relevant to the invention are disclosed. Applicant states that biliary transport protein that function to transport flavopiridol are members of the ABC protein family. Applicant states that the specification provides examples of ABC family members. Applicant states that the specification discloses that 1) flavopiridol is transformed to glucuronide which appears to be a polymorphic event, 2) variability in gluronidation of flavopiridol is mainly responsible for differential accumulation of flavopiridol in patients, 3) the presence of genetic polymorphism of flavopiridol glucuronidation in patients is indicated; 4) that these gene polymorphisms play a critical role in drug-related toxicity 5) variants

if UGT play a role in the polymorphic metabolism of flavopiridol and the role of the ABC family of proteins in the biliary transport of flavopiridol as regulators of flavopiridol toxicity. Applicant states that the present invention looks at UGT and ABC polymorphism thereof to assay, evaluate , detect or identify the role of those proteins in dictating flavopiridol toxicity to a patient. Applicant argues that the term "evaluating" is a specific activity and lakes clear how the claimed method operated to detect polymorphisms. Applicant states that one of ordinary skill in the art would know how to practice the invention. Finally, Applicant states that one of skill in the art would known what subject matter the claims encompass and that the claims as written makes clear the subject matter.

12. The arguments have been thoroughly reviewed and considered but they are not found persuasive for the reasons that follows: Firstly, the Examiner acknowledges Applicant's summary of the invention as taught by the specification, however it is noted that although the claims are interpreted in light of the specification, limitations from the specification are not read into the claims. See *In re Van Geuns*, 988 F.2d 1181, 26 USPQ2d 1057 (Fed. Cir. 1993). Additionally, the courts have established that during patent examination, the claims must be interpreted broadly as reasonably allow *(In re Zletz, 893 F.2d321-22, 13 USPQ2d 1320, 1322 (Fed. Cir. 1989)*. In this case, the claim as written in unclear because it cannot be determined if the recitation of "evaluating" is intended to require the practice of actual, active method steps or whether the claims might encompass solely metal steps of "evaluating" or "determining" or "identifying". For example, would the claims encompass method in which the UDGT1A9-encoding nucleic acid could be "evaluated" by reading a published sequence in an article or a datable and a polymorphism "evaluated" by comparing that

published sequence to another published sequence or to a Table, such that the claims read on a thought process? The claims as written only suggest a method for evaluating the nucleic acid sequence for a polymorphism. So once the polymorphism is "evaluated" in the UGT1A9- encoding nucleic acid, then what? Is the polymorphism detected? Is the polymorphism which is detected associated with a risk of flavopiridol-induced toxicity? The claim as written do not teach theses steps and thus it cannot be clearly determined Applicant's intend. Applicant's arguments are not sufficient to overcome the claim rejection. Accordingly, the rejection under 35 U.S.C. 112 second paragraph as being indefinite is maintained.

Conclusion

13. **THIS ACTION IS MADE FINAL.** Applicant is reminded of the extension of time policy as set forth in 37 CFR 1.136(a).

A shortened statutory period for reply to this final action is set to expire THREE MONTHS from the mailing date of this action. In the event a first reply is filed within TWO MONTHS of the mailing date of this final action and the advisory action is not mailed until after the end of the THREE-MONTH shortened statutory period, then the shortened statutory period will expire on the date the advisory action is mailed, and any extension fee pursuant to 37 CFR 1.136(a) will be calculated from the mailing date of the advisory action. In no event, however, will the statutory period for reply expire later than SIX MONTHS from the mailing date of this final action.

12. Any inquiry concerning this communication or earlier communications from the examiner should be directed to Examiner Cynthia Wilder whose telephone number is (703) 305-1680. The

examiner can normally be reached on Monday through Thursday from 9:30 am to 6:30 pm and on Friday from 9:30 am to 1:30 pm.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Gary Benzion, can be reached at (703) 308-1119. The official fax phone number for the Group is (703) 308-4242. The unofficial fax number is (703) 308-8724.

Any inquiry of a general nature or relating to the status of this application or proceeding should be directed to the Group's receptionist at (703) 308-0196.

Cynthia B. Wilder, Ph.D.

April 8, 2003

KENNETH R. HORLICK, PH.D
PRIMARY EXAMINER
4/10/03